

# Chapter 18

## Neonatal Conditions, with Emphasis on the Equine Neonate

Jeanne Lofstedt

### I. INTRODUCTION

**A.** Goals. Until recently, the focus of equine neonatology was on saving the critically ill foal. The emphasis has now shifted to evaluation of fetoplacental well-being during late gestation, with the goal being early identification and appropriate intervention in the case of an abnormal pregnancy or periparturient event. Owners, farm managers, and veterinarians should be cognizant of the findings that may indicate that the neonatal foal is at risk for future problems (Table 18-1) because early recognition and aggressive treatment of such foals generally improves their prognosis for survival and future athletic performance while at the same time decreasing overall treatment costs. If possible, high-risk mares should receive late-term fetal monitoring and be assured of an attended delivery with adequate resuscitation and stabilization of the foal after birth.

**B.** **Recognition of high-risk pregnancies.** Maternal conditions associated with a high-risk pregnancy are presented in Table 18-2. Mares experiencing problem pregnancies can usually be assigned to one of three categories:

1. Mares with histories of abnormal pregnancies, deliveries, or newborn foals
2. Mares at risk with the current pregnancy as the result of a systemic illness or a reproductive abnormality
3. Mares with no apparent risk factors that experience an abnormal periparturient event

**C.** **Outcomes for foals admitted to neonatal intensive care units**

1. Short-term outcomes have improved dramatically in the last two decades. Before 1980, fewer than 25% of foals presented to referral institutions for treatment were discharged alive. Foal units today quote overall success rates of greater than 70% for sick neonatal foals.
  - a. Diseases associated with particularly favorable short-term survival rates include hypoxemic-ischemic encephalopathy [HIE, neonatal maladjustment syndrome (NMS)], uroperitoneum, infectious and noninfectious diarrhea, and noninfectious musculoskeletal diseases (e.g., angular limb deformities, flexural deformities).
  - b. Diseases associated with poor short-term survival rates include established sepsis, sepsis accompanied by bacterial meningitis, septic arthritis, and septic osteomyelitis.
2. **Long-term outcome.** One of the major problems in conducting long-term follow-up is finding an appropriate population for statistical comparison. Most often, comparisons are made with half or full siblings, or to the patient population at a referral hospital; however, neither of these populations are representative of the general population.
  - a. Most of the common foal diseases seem to have little impact on the foal's ability to perform as an adult. Examples of diseases that appear to have little impact on future foal performance are HIE, severe bacterial lung disease, infectious and noninfectious diarrheas, uncomplicated umbilical diseases (e.g., omphalitis, patent urachus) and uroperitoneum.
  - b. There are three disease categories that negatively impact the long-term performance of surviving foals:
    - (1) Noninfectious orthopedic diseases

TABLE 18-1. Abnormalities Warranting Closer Evaluation of the Neonate

Abnormalities of Labor and Delivery	Abnormalities in the Neonate
Premature parturition or abnormally long gestation	Meconium-stained neonate
Prolonged labor	Twins
Dystocia	Orphaned foal
Induced labor	Dysmaturity or prematurity
Cesarean section	Delay or failure of colostrum ingestion
Premature placental separation	Trauma (birth, dam, predators)
Umbilical cord abnormality	Adverse environmental conditions
Placental abnormality (placentitis, edema, villous atrophy)	Congenital anomalies
	Weakness
	Failure to stand and nurse within 2–3 hours

- (2) Prematurity characterized by small stature and noninfectious orthopedic disorders (e.g., angular limb deformities, tarsal bone collapse)
- (3) Septic arthritis and osteomyelitis

## II. PREMATUREITY OR DYSMATURITY

### A. Introduction

1. Terminology. The literature abounds with terms for the neonatal foal with physical characteristics of immaturity: premature, immature, dysmature, intrauterine growth-retarded (IUGR), small for gestational age (SGA), ready or unready for birth, and viable or nonviable.
2. Criteria
  - a. Gestational age. Although most authors define a foal born before 320 days' gestation as premature (the mean gestation length of a Thoroughbred is 340 days), gestational age is only one of many criteria used to assess readiness for birth. Because gestation of mares is extremely variable, a 335-day fetus may be

TABLE 18-2. Maternal Conditions Associated With a High-Risk Pregnancy

Past History	Systemic Diseases	Reproductive Problems
Foals with NI, NMS, or congenital problems	Severe malnutrition	Severe endometrial fibrosis
Premature, septic, or hypoxic foals	Fever, endotoxemia, severe systemic infection	Hydrops allantiois or hydrops amnii
Dystocia or premature placental separation	Severe anemia or hypoproteinemia	Purulent vaginal discharge
Foal rejection	Gastrointestinal crises	Prepubic tendon rupture or abdominal hernia
Exposure to infectious diseases known to cause abortion (e.g., EHV-1, EVA)	Laminitis	Poor colostrum quality or premature lactation
	Musculoskeletal or CNS problems causing prolonged recumbency	Pelvic injuries

CNS = central nervous system; EHV-1 = equine herpesvirus-1; EVA = equine viral arteritis; NI = neonatal isoerythrolysis; NMS = neonatal maladjustment syndrome.

TABLE 18-3. Clinical Findings Suggestive of Immaturity

Gestation length less than 320 days
Weak suckle reflex, failure to nurse within 3 hours of birth
Failure to stand within 2 hours of birth
Low birth weight (less than 45 kg in Thoroughbreds or less than 10% of the dam's weight in other breeds)
Short, silky haircoat
Pliant ears and soft lips
Bulging, prominent forehead and eyes (especially in equine twins and other growth-retarded newborn foals)
Generalized weakness ("floppiness")
Increased passive range of motion of limbs
Marked flexor tendon laxity in the rear limbs
Hypothermia and difficulty thermoregulating
Intolerance to enteral feeding (abdominal pain)
Progressive tachypnea after birth with evidence of respiratory distress
Poor ossification of cuboidal bones in the carpi and tarsi

completely unprepared for birth if its normal gestational length was intended to be 365 days.

### b. Endocrine maturation

- (1) Normal physiology. The fetal pituitary–adrenal axis controls the final maturation of various organ systems, including the pulmonary system.
  - (a) Cortisol. The fetal adrenal gland is poorly responsive to adrenocorticotrophic hormone (ACTH) throughout most of pregnancy, but in the last 3–5 days of gestation, its sensitivity changes, resulting in a significant increase in fetal cortisol 24–48 hours before birth. This cortisol surge causes maturation of the hematopoietic system, resulting in a total white blood cell (WBC) count of more than 5000 cells/ $\mu$ L in the healthy term foal immediately after birth.
  - (b) Thyroid hormone. The triiodothyronine ( $T_3$ ) concentration in the healthy term foal is 10–20 times that of an adult horse. Thyroid hormone in the neonatal foal is required for thermogenesis, skeletal maturation, and may act synergistically with cortisol to cause normal lung maturation.
- (2) "Unready for birth" foals. Foals removed suddenly from the uterus before final endocrine maturation has taken place (e.g., by a poorly timed cesarean section) have low serum concentrations of cortisol and thyroid hormone and, when challenged with exogenous ACTH, do not respond with appropriate increases of cortisol. They have incomplete body system maturation and generally adjust poorly to extrauterine life.
- (3) "Immature but ready for birth" foals. Maturation is often hastened in foals exposed to chronic *in utero* stress (e.g., chronic placentitis) during gestation. Despite having characteristics of physical immaturity, foals stressed in *utero* have adequate pulmonary and hematologic function and cope well with extra-uterine life.

### B. Clinical finding are summarized in Table 18-3.

### C. Complications

1. Respiratory difficulties are attributed to a number of factors, including dependent lung atelectasis caused by lung and chest wall immaturity, in utero-acquired pneumonia, and lack of mature surfactant.

2. Abnormal glucose homeostasis. Premature foals have a significantly lower blood glucose concentration than full-term foals and are less able to maintain stable glucose concentrations in the first 2 hours postpartum. Low hepatic glycogen stores, immature glycogenolytic mechanisms, and a blunted insulin response all contribute to abnormal glucose homeostasis in the premature newborn.
3. Angular limb deformities. Because ossification of the cartilaginous cuboidal bone precursors to the carpal and tarsal bones occurs in the last 2–3 weeks of gestation, the premature or dysmature foal that ambulates may experience collapse of these bones, which may in turn result in angular limb deformities.
4. Corneal ulceration. Entropion, leading to corneal irritation and ulceration, is a common complication experienced by the premature or immature foal.
5. Patent urachus. In the fetus, the urachus drains urine from the bladder into the allantoic sac. In late gestation, some urine is diverted to the amniotic sac via the urethra, and at the time of delivery (immediately after umbilical cord rupture), the abdominal musculature around the umbilicus contracts, resulting in cessation of urine flow from the urachus. Failure for this closure to occur in the immediate postpartum period leads to the development of a congenital patent urachus.

**D.** Therapeutic plan. Frequent and comprehensive clinical and laboratory evaluation of all body systems is required to detect and address deterioration in neurologic status, cardiorespiratory function, and renal function of the immature neonatal foal. General supportive care is necessary.

1. Prevention of decubital ulcers and scalding
  - a. An air mattress or cushions help prevent decubital ulcers. A foal that is unable to maintain sternal recumbency or stand should have an attendant present to keep it in sternal recumbency, turn it from side-to-side every 2 hours, and assist it in standing as needed.
  - b. Scalding by feces and urine can be minimized by covering the bedding with absorbent pads.
2. Prevention of nosocomial infection. Foals should be separated from the adult horse population and high-traffic areas, and strict hygiene and cleanliness should be maintained in the foal ward to decrease the risk of nosocomial infections.
3. Prevention of **hypothermia**. The ambient temperature can be increased using radiant heat lamps, hot water pads, blankets, and warmed intravenous fluids.
4. Nutritional support. Premature or dysmature foals are often unable to suckle from the mare and have to be fed via a bottle, bucket, or nasogastric tube.
  - a. Frequency and amount. It is important to remember that the healthy foal nurses as frequently as 7 times/hour and consumes 16%–28% of its body weight/day (155 ml/kg/day) in milk. Initially, the premature foal should receive 10% of its body weight in milk, divided into at least 12 feedings over 24 hours; if the foal tolerates this amount, the volume fed can be increased gradually until the foal receives 20%–25% of its body weight in milk. Unfortunately, many immature foals do not tolerate large volumes orally (i.e., they develop colic or diarrhea) and partial or total parenteral nutrition may have to be implemented.
  - b. Methods
    - (1) Bottle feeding. A lamb nipple can be used to bottle feed a foal. A foal with a weak suckle reflex should never be bottle fed because aspiration pneumonia and malnutrition may ensue. Mare's milk is the optimal milk source. There are a number of commercially available mare milk replacers and many foals appear to thrive on goat milk. Hypoglycemic foals (i.e., those with a glucose concentration of less than 40 mg/dl) should receive intravenous dextrose (5%–10%) in addition to oral alimentation.
    - (2) Nasogastric intubation. A small-diameter nasogastric tube is placed in the distal esophagus. The foal can nurse from the mare while the tube is in place.
    - (3) Bucket feeding. Foals are easily taught to drink milk from a shallow pan or bucket. The foal should be encouraged to suckle a clean finger which is then gradually lowered into the bucket containing the milk.

- (4) Parenteral nutrition. Essentially, parenteral nutrition involves constant intravenous infusion of a hypertonic solution containing various concentrations of dextrose, amino acids, lipids, electrolytes, and vitamins.
  - (a) Parenteral solutions should be mixed under a hood wearing sterile gloves and a mask to prevent contamination. They are generally administered via a nontrombogenic jugular catheter and a dedicated line. Fluid administration rates are carefully controlled and fluid lines and hanging bags are changed daily.
  - (b) Patients receiving parenteral nutrition should continue to receive small-volume enteral feeding if at all possible.
  - (c) The patient should be monitored frequently to detect complications. Potential complications include hyperglycemia, hyperlipidemia, metabolic acidosis, hypokalemia, and infection at the catheter site.
5. Immunologic support. Failure of passive transfer (FPT) of colostral immunoglobulins (see IV) is a common occurrence in the premature or dysmature foal. Good-quality colostrum should be fed within 6 hours of birth, and passive transfer status should be assessed when the foal is 18–24 hours old. Plasma should be transfused if the immunoglobulin G (IgG) concentration is less than 800 mg/dl.
6. Antimicrobial treatment. Many premature births are associated with infections acquired in *utero*. Broad-spectrum bactericidal antimicrobials should be used prophylactically in all premature foals (see V E 2).
7. Cardiovascular support
  - a. Dehydration and hemoconcentration. Foals should be treated intravenously with an isotonic balanced electrolyte solution (e.g., lactated Ringer's solution, 40–60 ml/kg/day).
  - b. Acidemia is defined as a blood pH of less than 7.3. Foals with acidemia should be adequately ventilated and receive 1.3% (isotonic) sodium bicarbonate intravenously.
8. Respiratory support. Most immature foals have some pulmonary dysfunction.
  - a. **Atelectasis** (as a result of lung and chest wall immaturity) can often be managed by simply maintaining the foal in sternal recumbency, turning it frequently, and encouraging lung expansion through stimulating deep breathing or coughing.
  - b. Hypoxia is defined as an arterial oxygen tension ( $P_{aO_2}$ ) of less than 70 mm Hg with a normal arterial carbon dioxide tension ( $P_{aCO_2}$ ). Hypoxic foals often benefit from humidified oxygen administered via face mask or nasal insufflation at a rate of 5–10 L/min.
  - c. Hypercapnia is defined as a  $P_{aO_2}$  of less than 65 mm Hg and a  $P_{aCO_2}$  of greater than 65 mm Hg. Hypercapnic foals benefit from assisted or controlled ventilation via orotracheal or nasotracheal intubation.
  - d. Lack of **surfactant**. Surfactant replacement has been utilized in an attempt to increase survivability of the premature foal with immature lung surfactant. There are anecdotal reports that this treatment modality is beneficial, but large-scale controlled studies have not been undertaken.
9. **Musculoskeletal** support
  - a. Foals with radiographic evidence of incomplete carpal and tarsal bone ossification should be housed in a small stall to restrict exercise.
  - b. Excessive flexor tendon laxity can be managed with physical therapy and the application of heel extensions to the bottom of the foot. Support wraps should be light and used sparingly because they may exacerbate tendon laxity.
10. Treatment of other complications
  - a. Corneal ulcer. Affected foals should be treated with topical antibiotics, mydriatics, and vertical mattress sutures to evert the eyelid.
  - b. Patent urachus. Treatment includes chemical cautery or surgical excision (see VI B 4).
  - c. Adrenal insufficiency. Treatment is controversial and reserved for those foals with laboratory evidence of adrenocortical insufficiency.

- (1) Physiologic doses of glucocorticoids (e.g., 50 mg of hydrocortisone succinate) have been used.
- (2) Administration of **long-acting** synthetic ACTH at a total intramuscular dose of 0.4 mg, followed by a 0.2-mg dose 6 and 12 hours later, has been advocated as well.

**E.** Prognosis. The periparturient history, laboratory testing, and observation of clinical progression over the first 2 days can be used to develop a prognosis for the premature or immature foal.

#### 1. Periparturient history

- a. Foals delivered early and abruptly by induction of parturition, cesarean section, or because of severe systemic maternal illness in the mare generally have a poor prognosis. They do not experience the endocrinologic events required for normal maturation, are "unready for birth," and the prognosis for survival is poor (survival rate of 20%–25%).
- b. Foals delivered naturally, but prematurely, by a healthy mare usually have a fair prognosis. With appropriate supportive care, survival rates as high as 70% are possible. Close inspection of the placenta from these deliveries may reveal villous atrophy or placentitis. Placental pathology is thought to interfere with uteroplacental blood flow, imposing chronic *in utero* stress, maturation of the fetal pituitary–adrenal axis, and "readiness for birth."

#### 2. Laboratory testing can be used to assess readiness for birth.

- a. Assessment of electrolyte concentrations in prepartum mammary secretions. The electrolyte concentrations in prepartum mammary secretions change dramatically shortly before the mare foals down. A calcium concentration greater than 40 mg/dl is a reasonable indicator of readiness for birth and can be used to determine if the time is appropriate for elective induction or a cesarean section.
  - (1) At term, calcium and potassium concentrations in mammary secretions increase to greater than or equal to 40 mg/dl and 35 mEq/L, respectively, whereas the sodium concentration decreases to less than or equal to 30 mEq/L.
  - (2) Before 310 days' gestation, elevated milk calcium levels indicate placental pathology, not fetal maturity. Changes in milk sodium and potassium concentrations do not occur in mares with placentitis; therefore, fetal maturation is most accurately assessed by measuring **concentrations** of all three **electrolytes**.

#### b. Routine laboratory testing

##### (1) Complete blood count (CBC)

- (a) Foals with a total WBC count of greater than 5000 cells/ $\mu$ L on day 1 of life (or a low WBC count on day 1 that increases to greater than 5000 cells/ $\mu$ L on day 2 or 3) generally have a favorable prognosis.
- (b) Foals with a neutrophil–lymphocyte ratio that is greater than 2 on day 1, or low on day 1, but increases to greater than 2 on day 2 or 3, have a fair prognosis.
- (c) Persistent leukopenia and **neutropenia** usually indicate that the foal is endocrinologically immature and will be a **nonsurvivor** in the postnatal period.

- (2) Fibrinogen concentration. A plasma fibrinogen concentration that exceeds 400 mg/dl at birth is generally associated with a favorable prognosis. It suggests that an *in utero* infection caused the premature delivery. As mentioned previously, foals stressed *in utero* generally adjust better in the early neonatal period.
- (3) Blood gas analysis. Nonviable premature foals usually have a metabolic acidosis with a blood pH persistently less than 7.3.

#### c. Endocrinologic testing

- (1) **Serum** cortisol. A plasma cortisol concentration of 120–140 mg/ml within 2 hours of birth indicates readiness for birth, whereas a value of less than 30 mg/ml suggests poor adrenal function and an unfavorable prognosis.

- (2) ACTH response test. Foals that are endocrinologically mature respond with a two-fold increase in plasma cortisol and a widening of the neutrophil–lymphocyte ratio in response to the administration of short-acting exogenous ACTH (0.125 mg, intramuscularly).

#### 3. Careful assessment of clinical progression over the first 2 days of the immature foal's life can also be used to formulate a prognosis:

- a. In "unready for birth" foals, the first 12–18 hours after resuscitation are deceptively uneventful. However, progressive deterioration in neurologic function and an inability to maintain homeostasis soon develop. Death is certain without aggressive intensive care and the prognosis is poor. Some of the abnormalities exhibited by these foals are:
  - (1) Systemic weakness, depression, and seizures
  - (2) Intolerance to enteral feeding, resulting in abdominal distention, **colic**, and enterogastric **reflux**
  - (3) Declining pulse quality, subcutaneous edema, and **oliguria**
  - (4) Respiratory distress leading to respiratory **acidosis**
- b. A "ready for birth" foal that is born prematurely following exposure to chronic *in utero* stress usually progresses as follows:
  - (1) The foal is weak initially and requires assistance to stand.
  - (2) The foal's suckle reflex and appetite are reduced and it must receive milk and colostrum via a nasogastric tube.
  - (3) The foal has difficulty regulating its blood glucose level and body temperature.
  - (4) After 24 hours of supportive care, the foal gains strength, its mentation improves, and its appetite for milk often exceeds that of the normal foal.

4. Other factors influencing outcome include the **actual** birth weight of the foal (generally, the lower the birth weight, the poorer the prognosis), the presence of other complicating factors in the perinatal period (e.g., *in utero*–acquired infection or peripartum asphyxia), and the resources available for **treatment**.

### III. ACUTE PERINATAL ASPHYXIA

#### A. Introduction

1. Asphyxia is defined as decreased tissue oxygenation and can be caused by **hypoxemia** (decreased blood oxygen content) or **ischemia** (decreased blood flow).
2. Acute perinatal asphyxia is a multisystemic disease, affecting the nervous, cardiovascular, gastrointestinal, and renal systems of the neonate. Because central nervous system (CNS) signs are noticed first and are the most overt, perinatal asphyxia initially was not recognized for the multisystemic disease that it really is. A variety of terms were used to describe the disease in affected foals based on the most salient neurologic deficits (e.g., barkers, wanderers, dummies, **convulsives**). In 1968, the term "neonatal maladjustment syndrome" (**NMS**) was coined to describe foals exhibiting gross behavioral disturbances and failure to adapt in the perinatal period. Ischemic–hypoxemic brain damage was suspected to be the cause of **NMS**.

**B.** Clinical findings. Perinatal asphyxia produces an array of clinical abnormalities. The clinical picture is influenced by the maturity of the foal at birth and the severity and duration of the **asphyxial** episode. Neurologic signs predominate; however, careful assessment usually reveals involvement of other organ systems.

#### 1. Neurologic signs

- a. Affected foals often appear outwardly normal for the first 12–24 hours. Loss of dam recognition, loss of suckle reflex, aimless wandering, and head pressing are the first signs observed in asphyxiated neonatal foals.

- b. Severely affected foals may exhibit bruxism; abnormal vocalization; hyperexcitability; extensor spasms of the limbs, neck, and tail; and convulsions alternating with a semicomatose unresponsive state. Dysphagia, central blindness, anisocoria, nystagmus, head tilt, proprioceptive deficits, and spasticity have also been reported.
- 2. Respiratory signs. Foals with respiratory dysfunction exhibit varying degrees of tachypnea and dyspnea. Erratic, abnormal breathing patterns are also observed with some frequency.
- 3. Cardiovascular signs. Dysfunction may manifest as tachycardia, signs of hypotension, or murmurs associated with valvular insufficiency.
- 4. Renal signs include oliguria and peripheral edema if fluid therapy is not adjusted for decreased urine output.
- 5. **Gastrointestinal** signs are ileus, poor feeding, colic, lethargy, abdominal distention, delayed gastric emptying, gastric reflux, and diarrhea. Reflux fluid and feces often test positive for occult blood. Colic, hemorrhagic diarrhea, and sudden death have been reported in severe cases.

### C Etiology and pathophysiology

- 1. Etiology. A variety of fetal and maternal conditions are associated with perinatal asphyxia.
  - a. Fetal factors include twinning, meconium aspiration, sepsis, prematurity or dysmaturity, and severe anemia.
  - b. Maternal factors include conditions that cause hypotension or impaired tissue oxygenation (e.g., endotoxemia, anemia, hemorrhagic shock), maternal surgery or cesarean section, and placental abnormalities (e.g., those caused by ingestion of endophyte-infested fescue during pregnancy, placental infection, or premature placental separation).
- 2. Pathophysiology
  - a. Shunting. Initially, the fetus responds to asphyxia by shunting blood away from nonvital organs (e.g., the gut, kidneys, bone, muscle, and skin) to vital organs (e.g., the brain, heart, and adrenal gland).
    - (1) Mild asphyxia causes a mild decrease in heart rate and a slight increase in blood pressure, but little change in cardiac output.
    - (2) With severe asphyxia, the heart rate, cardiac output, and blood pressure decrease as oxidative phosphorylation fails and energy reserves in cardiac muscle are depleted.
  - b. Metabolic derangements. Without sufficient energy, cellular ion pumps in various body tissues eventually fail, resulting in intracellular accumulation of sodium, chloride, water, and calcium and extracellular accumulation of excitatory neurotransmitters in the brain (e.g., glutamate).
    - (1) Glutamate accumulation in the brain after an ischemic event apparently causes excessive stimulation of cell surface receptors, eventually resulting in neuronal death.
    - (2) Intracellular free calcium accumulation causes cell death in several ways, including activation of enzyme systems that attack the structural integrity of the cell and impairment of mitochondrial function.
    - (3) Oxygen free radicals are generated during the reperfusion phase that follows a hypoxemic-ischemic insult. Oxygen free radicals cause membrane fragmentation by attacking the lipids in cell membranes and are in part responsible for the increased capillary permeability, edema formation, and tissue damage, that occur following restoration of blood flow to previously ischemic tissues.
  - c. **Sequelae**
    - (1) Neurologic effects. In the brain, asphyxia can lead to HIE accompanied by edema, necrosis, and hemorrhage.
    - (2) Cardiac effects. The effects of perinatal asphyxia on myocardial function can be profound. Decreased myocardial contractility and congestive heart failure

(CHF) are common sequelae and may be associated with infarcts in myocardial and papillary muscles. The systemic hypotension caused by these lesions further contributes to tissue hypoxia, development of metabolic acidosis, and decreased renal perfusion in the asphyxiated neonate.

- (3) Pulmonary effects. The neonatal pulmonary system responds to hypoxemia and acidosis by reflex vasoconstriction, which, in turn, causes an increase in pulmonary vascular resistance, pulmonary hypertension, and increased right atrial pressure.
  - (a) If pulmonary arterial pressure exceeds systemic pressure, right-to-left flow through the ductus arteriosus and foramen ovale may result in reestablishment of persistent fetal circulation characterized by severe hypoxemia unresponsive to oxygen therapy.
  - (b) Decreased pulmonary blood flow may cause decreased delivery of lipid precursors to the lung, resulting in decreased surfactant production.
  - (c) Meconium aspiration, a common sequela of birth asphyxia, usually initiates a chemical pneumonitis that can further compromise pulmonary function.
  - (d) Perinatal asphyxia may decrease the responsiveness of respiratory centers in the brain, causing periods of apnea or abnormal breathing.
- (4) Renal effects. Redistribution of blood flow away from the kidneys causes decreased renal perfusion and, frequently, acute renal tubular necrosis and oliguria.
- (5) Gastrointestinal effects. Reduced intestinal blood flow during an asphyxial episode causes variable degrees of bowel ischemia.
  - (a) Mild signs of gastrointestinal dysfunction are commonly exhibited by asphyxiated foals, including meconium impactions and intolerance to enteral feeding manifested as abdominal distention, colic, diarrhea, or delayed gastric emptying.
  - (b) Severe ischemia causes total loss of bowel integrity, resulting in overwhelming bacteremia and septic shock.
- (6) **Other** effects. Severe asphyxia may lead to anoxic liver damage, necrosis and dysfunction of endocrine organs, and coagulopathy. To date, these disorders have not been described in asphyxiated equine neonates.

### D. Diagnostic plan

- 1. **Physical** examination. An in-depth physical examination is indicated for all recumbent foals to:
  - a. Provide baseline information against which foal progress can be compared
  - b. Aid in the identification of subtle but important abnormalities that may be overshadowed by grossly obvious clinical signs, such as seizures
- 2. Baseline clinicopathologic information should be gathered. A CBC and blood culture should be ordered, and passive transfer status should be assessed. A sepsis score (see V D 3) should be calculated.
- 3. Specific assessments
  - a. Neurologic assessment. Neurologic signs caused by HIE need to be distinguished from those caused by meningitis, hypoglycemia, or congenital anomalies.
    - (1) Cerebrospinal fluid analysis allows differentiation of meningitis and HIE (meningitis is characterized by an increased leukocyte count and protein concentration).
    - (2) imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), are being used with increasing frequency to document location, severity, and progression of brain injury in asphyxiated large animal neonates.
  - b. Respiratory assessment
    - (1) Arterial blood gas analysis usually reveals hypoxemia, hypercarbia, and acidemia. These are typical findings in a foal with hypoventilation; affected foals usually respond dramatically to nasal oxygen insufflation. In contrast, foals with persistent fetal circulation do not respond to inspired oxygen.

- (2) Thoracic radiography is always indicated for foals with birth asphyxia.
  - (a) In cases of pulmonary hypertension, thoracic radiographs may reveal pulmonary hypoperfusion (clear lung fields with decreased pulmonary vascular markings).
  - (b) Surfactant deficiency results in diffuse lung atelectasis and a diffuse reticulogranular radiographic appearance with air bronchograms.
  - (c) Meconium aspiration results in patchy perihilar infiltrates, focal areas of atelectasis, and hyperaeration.
- c. Cardiovascular assessment
  - (1) Electrocardiography and echocardiography may be indicated in foals with murmurs or cardiac dysrhythmias. Echocardiography may reveal persistent fetal circulation.
  - (2) Determination of cardiac isoenzyme activities is necessary to detect myocardial necrosis.
- d. Renal assessment. Renal function is assessed by measuring urine output, performing a urinalysis, and assessing the results of a biochemistry profile. Typical findings include oliguria (a urine output of less than 2 ml/kg/hr), azotemia, and electrolyte disturbances such as hypocalcemia, hyponatremia, hypochloremia, and hyperkalemia.
- e. **Gastrointestinal** assessment. Gastrointestinal dysfunction is primarily diagnosed based on clinical signs. The most severe form of gastrointestinal dysfunction associated with birth asphyxia, necrotizing enterocolitis (NEC), can be diagnosed radiographically based on the presence of submucosal gas accumulation in the bowel wall (pneumatosis intestinalis).

**E. Differential diagnoses.** Conditions such as neonatal sepsis, meconium aspiration, prematurity, and hypoglycemia can mimic perinatal asphyxia. Perinatal asphyxia can also be a complicating factor in many of these conditions.

**F. Therapeutic plan.** Therapeutic goals are numerous and address the multiple organ failure that is present.

1. Treatment of CNS dysfunction includes seizure control, nursing care to prevent trauma, fluid therapy, nutritional support, and control of cerebral edema.
  - a. Seizure control
    - (1) Diazepam (0.11–0.44 mg/kg intravenously) has a rapid onset of action and is used for initial seizure control.
    - (2) Pentobarbital (2–10 mg/kg intravenously every 12 hours) can be used to manage severe or repeated seizures. Serum concentrations of pentobarbital should be monitored.
    - (3) Xylazine and acepromazine should not be used to control seizures. Xylazine causes transient hypertension and may exacerbate cerebral hemorrhage, and acepromazine lowers the seizure threshold.
  - b. Control of cerebral edema. Cerebral edema occurs in some asphyxiated foals and is treated with dimethylsulfoxide (DMSO; 0.5–1.0 g/kg administered over 1–2 hours as a 10%–20% solution) and/or mannitol, an osmotic diuretic (0.25–1.0 g/kg given as a 20% solution slowly over 1–2 hours). Mannitol may exacerbate CNS hemorrhage; therefore, it should be used with extreme caution in asphyxiated neonates.
  - c. Prevention of trauma. Leg wraps, a padded helmet, and a padded stall may be required to protect the asphyxiated neonate from self trauma.
2. Treatment of respiratory dysfunction includes maintenance of oxygenation and ventilation of the patient.
  - a. Treatment of hypoxia. Hypoxia is usually corrected by administering humidified oxygen (3–10 L/min) via nasal insufflation and keeping the foal in sternal recumbency.
  - b. Treatment of hypercapnia. Respiratory center depression can cause hypercapnia, characterized by a  $P_{aO_2}$  of less than 65 mm Hg and a  $P_{aCO_2}$  greater than 65 mm Hg.

- (1) Positive-pressure ventilation may be required for treatment of recurrent apnea, severe respiratory center depression, or diffuse pulmonary atelectasis caused by surfactant deficiency.
- (2) If respiratory center depression is causing inappropriate control of breathing, methylxanthines (e.g., theophylline or caffeine) can be used to stimulate respiratory neuronal activity and increase responsiveness to hypercapnia.
  - (a) The recommended dose of caffeine is a loading dose of 10 mg/kg and a maintenance dose of 2.5 mg/kg/day.
  - (b) Methylxanthines have a narrow therapeutic range and they should be discontinued if signs of toxicity are noted (e.g., agitation, seizures, tachycardia, hypotension, colic, diarrhea).
- c. Treatment of pulmonary atelectasis. Intratracheal surfactant administration has been recommended by some authors.
3. Treatment of cardiac dysfunction revolves around judicious use of intravenous fluids (see III F 6 a) and the administration of inotropes.
  - a. Dopamine or dobutamine (infused at a rate of 2–10 µg/kg/min) may be used to increase cardiac output and improve tissue perfusion.
  - b. Diuretics (e.g., furosemide) may be used to treat the edema associated with cardiac failure.
  - c. Digoxin (0.02–0.035 mg/kg orally every 24 hours) should be used if there is evidence of cardiac failure.
4. Treatment of renal dysfunction involves judicious use of intravenous fluids, diuretics, and administration of low doses of dopamine to stimulate dopaminergic receptors. Fluid input and urine output should be carefully monitored to avoid overhydration.
  - a. Dopamine infusions (2–4 µg/kg/min) have been advocated to improve renal blood flow and urine output.
  - b. Diuretics. Serum electrolyte concentrations should be carefully monitored during diuretic therapy.
    - (1) Furosemide infusions of 0.25–2.0 µg/kg/min have been used successfully to treat oliguric renal failure in asphyxiated foals. Furosemide acts synergistically with dopamine to produce renal vasodilation and diuresis.
    - (2) Mannitol therapy may be added if oliguria persists after dopamine and furosemide administration.
  - c. Dobutamine therapy should be instituted if cardiac dysfunction appears to be causing systemic hypotension and renal hypoperfusion.
5. Treatment of gastrointestinal dysfunction. Gastrointestinal dysfunction is treated with decompression, the use of prokinetic agents, or both.
  - a. Nasogastric decompression. If the foal has delayed gastric emptying and decreased intestinal motility, nasogastric decompression can be used to relieve fluid and gas accumulation. Severe, persistent large bowel distention may respond to percutaneous trocarization using sterile technique and a 16- or 18-gauge catheter.
  - b. Prokinetic agents, such as metoclopramide (0.25–0.3 mg/kg by intravenous infusion) or erythromycin (5–10 mg/kg orally or by intravenous infusion) may improve gastric emptying and small intestinal motility.
6. General supportive care
  - a. Fluid therapy. Polyionic isotonic fluids should be used to correct dehydration and expand blood volume. To avoid overhydration, asphyxiated foals should be carefully monitored using clinical assessment of hydration and monitoring of body weight changes and urine output. Normal urine output is 6–7 ml/kg/hr; measures should be introduced to improve urine output if it decreases to less than 2 ml/kg/hr.
    - (1) Patients with metabolic acidosis should receive supplemental bicarbonate based on results of blood gas analysis. Caution should be exercised when bicarbonate is given to foals with severe respiratory compromise, because in

these foals, bicarbonate can worsen the acidosis because of carbon dioxide retention.

(2) Specific electrolyte abnormalities should also be corrected with fluid therapy.

b. **Immunologic** support. The plasma immunoglobulin concentration should be measured and colostrum or plasma administered if the foal's serum IgG levels are less than 800 mg/dl.

c. Nutritional support

(1) Nasogastric tube. Foals that are unable to nurse from the mare or a bottle should be tube fed using the recommendations given in II D 4.

(2) **Parenteral** nutrition. If gut function is questionable, parenteral nutrition should be employed. To minimize the risk of NEC, foals that have suffered severe asphyxia complicated by hypotension or hypothermia should not receive any enteral feeds until their vital signs are stable.

(3) Enteral feeding should be initiated gradually and mare's colostrum or milk should be fed preferentially.

d. Antibiotic therapy. Broad-spectrum bactericidal antimicrobial therapy should be given to all asphyxiated foals because sepsis commonly accompanies ischemic bowel damage.

e. Antilulcer medication (e.g., ranitidine, sucralfate) is recommended for asphyxiated foals because gastric ulceration is a common complication.

### G. Prognosis

1. The prognosis is usually good for a term foal delivered without obvious complications, particularly if the foal was able to stand for period of time after delivery and had a normal immunoglobulin concentration at 18–24 hours of age. Approximately 75% of foals with good prognostic signs recover with intensive nursing care. In survivors, the clinical signs usually stabilize at 48–72 hours and their condition is significantly improved by 72–96 hours of age. Full recovery can take as long as 2 weeks.
2. The following findings are associated with a poor prognosis:
  - a. Concurrent septicemia
  - b. Failure to show any improvement in neurologic function by 5 days of life
  - c. A persistent comatose state or severe, recurrent seizures
3. Rare long-term neurologic sequelae may include unusually docile behavior as an adult, prolonged vision impairment, residual spasticity, or recurrent seizures.

## IV. FAILURE OF PASSIVE TRANSFER (FPT)

### A. Introduction

1. Incidence. FPT (i.e., inadequate transfer of colostral immunoglobulin) is widespread in both equine and bovine neonates, with reported prevalences of 2.9%–25% and 15%–68%, respectively. FPT also occurs in lambs, goat kids, and piglets, but the exact prevalences are unknown.
2. Neonatal immunity, colostrum production, and absorption of immunoglobulin. Neonates are capable of mounting an immune response at birth, but it is a primary response characterized by a prolonged lag period and production of low concentrations of antibody. Leukocytes of newborn animals exhibit reduced phagocytic and bactericidal activity as a result of fetal glucocorticoid production shortly before birth. Furthermore, the neonate's serum is deficient in some complement components, resulting in poor opsonic activity. Placental transfer of immunoglobulin does not occur to any extent in neonatal ungulates; therefore, they rely on colostral transfer of immunoglobulin to protect them against infectious disease early in the neonatal period. Colostrum is composed of immunoglobulins, immunologically active cellular components (lymphocytes, macrophages, polymorphonuclear cells) and nonspecific immune factors (lactoferrin, lysozyme, and complement).

a. Colostral immunoglobulin secretion occurs primarily via receptor-associated selective uptake of IgG from the maternal blood stream, transcellular transport, and release into lacteal secretions via the mammary epithelium. Colostral secretion takes place during the last 2–4 weeks of gestation and is regulated by hormonal changes that take place in late gestation.

b. Colostral absorption. Because of the low proteolytic activity in the digestive tract of newborns and the presence of trypsin inhibitors in the colostrum, colostral proteins are not degraded as a food source. Instead, they reach the small intestine, where the colostral immunoglobulins and other macromolecules are actively absorbed by specialized enterocytes through the process of pinocytosis.

(1) The "window" of gut absorptive capacity for macromolecules is narrow, lasting from birth to 18–24 hours of age with a significant decline after 6 hours of age. Reduced absorptive capacity after 6 hours is attributed to shedding of the specialized enterocytes and replacement by mature cells incapable of pinocytosis.

(2) Peak serum immunoglobulin concentrations are achieved 12–24 hours after birth; after this period, passively acquired antibody concentrations decline through normal catabolic processes.

### 3. General causes and consequences

a. Causes. FPT usually is attributed to one of three factors:

- (1) Poor colostral quality or quantity (i.e., the failure of the dam to produce colostrum in sufficient amounts or of sufficient quality)
- (2) Ingestion failure (i.e., the failure of the neonate to ingest sufficient amounts of colostrum early in the neonatal period)
- (3) Absorption failure (i.e., failure of the neonate to absorb adequate amounts of colostrum from the gastrointestinal tract into the systemic circulation)

b. Consequences of FPT

(1) Increased infectious disease morbidity and mortality. FPT generally increases morbidity and mortality associated with infectious disease (e.g., septicemia, diarrhea, pneumonia) in cattle herds, and it is generally accepted that foals with FPT are at a higher risk of developing septicemia.

(a) The consequences of FPT depend on the pathogen load in the environment and whether specific antibody to offending pathogen is present.

Considerable confusion was created by one equine study where no association between FPT and morbidity/mortality was demonstrated in foals in the first 3 months of life. The results of this study were later attributed to a scrupulous environment and the fact that the mares were allowed time to adjust to the broodmare farm environment prior to foaling.

(b) In herds with a high prevalence of septicemia, predisposing factors that should be considered in addition to FPT include unhygienic management practices, the presence of virulent pathogens, concurrent stress or disease, and lack of specific antibody.

(2) Increased duration of pathogen shedding. FPT may increase the duration of pathogen shedding in calves with diarrhea.

(3) Decreased weight gain. FPT has been shown to decrease weight gain of heifers up to 180 days of age.

(4) Starvation. Because ovine colostrum supplies a considerable amount of energy, lambs that fail to ingest colostrum may starve to death rather than exhibit signs of septicemia.

(5) Decreased milk production. FPT has been shown to affect milk production of heifers into their first lactation.

### B. Etiology

#### 1. FPT in foals

a. Poor colostral quality or quantity

(1) Maternal age. The foals of dams older than 15 years are at increased risk for FPT as a result of poor colostral quality.

(2) Leakage of colostrum (premature lactation) results in decreased colostral IgG

concentration. Factors leading to premature lactation are poorly understood, but twinning, premature placental separation, and placentitis have been incriminated.

- (3) Severe maternal illness and the ingestion of endophyte-infested fescue have been associated with decreased colostrum volume, quality, or both.
  - (4) Premature foaling (either from natural causes or induction) can lead to colostrum of insufficient quantity, quality, or both, because time and hormonal preparation for colostrum production were inadequate.
  - b. Ingestion failure
    - (1) Foal rejection of the mare (e.g., as a result of maternal illness or poor mothering ability) results in delayed colostrum ingestion.
    - (2) Neonatal weakness or musculoskeletal problems (e.g., flexural deformities) can make it difficult for the foal to ambulate and ingest adequate amounts of colostrum within the appropriate time frame.
  - c. Absorption failure. FPT is common in premature foals, even when they receive sufficient amounts of good-quality colostrum in the early postpartum period. Inefficient immunoglobulin absorption from the immature gastrointestinal tract, distribution and catabolism of IgG in foals that are already septic, and exposure to increased concentrations of exogenous or endogenous glucocorticoids (which would accelerate enterocyte maturation) have been incriminated as factors leading to FPT in these foals.
2. FPT in calves
- a. Poor colostrum quality or quantity
    - (1) First lactation. It is generally accepted that heifers in their first lactation produce less total colostrum containing less total immunoglobulin than cows in later lactations.
    - (2) Holstein breed. Colostrum quality may be affected by breed. Beef cattle generally produce colostrum with a high immunoglobulin concentration and Jersey cows have excellent colostrum quality. In contrast, Holstein cows have notoriously poor colostrum quality.
    - (3) Colostrum volume greater than 85 kg at first milking. In general, the larger the volume of colostrum produced, the lower the immunoglobulin concentration. If the first-milking colostrum of dairy cows that produce more than 8.5 kg of colostrum is discarded, more than 77% of the remaining colostrum will have sufficient IgG to ensure adequate passive transfer (if sufficient volumes are fed in a timely fashion).
    - (4) Premature calving or induction of parturition. Because colostrum secretion only occurs in the last month of gestation under hormonal influence, premature parturition or a shortened dry period fail to allow for optimum colostrum production. Premature induction of parturition may also decrease colostrum quality. Prostaglandin administration reduces the IgG concentration, and glucocorticoids apparently decrease the volume of colostrum that is produced.
    - (5) Premilking or premature lactation. The mammary gland only secretes a finite amount of colostrum; therefore, prepartum loss of colostrum via premilking or premature lactation will likely reduce postpartum colostrum quality.
    - (6) Delay in obtaining first-milking colostrum. If milking of colostrum from the mammary gland is delayed after calving, the colostrum will be diluted by secretion of milk into the mammary gland and have a low immunoglobulin concentration.
    - (7) Colostrum handling (pooling, repeated freezing and thawing).
      - (a) Colostrum pools created by mixing colostrum from different dams generally have lower immunoglobulin concentration than fresh colostrum and calves fed from these pools frequently do not achieve satisfactory passive transfer. There are several explanations for this:
        - (i) It is likely that colostrum from the second milking and beyond is contributed to the colostrum pool.
        - (ii) Colostrum from cows producing large volumes of inferior quality colostrum are more likely to be added to the pool.

(b) Processing of colostrum may affect the quality. Repeated freezing and thawing cycles or overheating of colostrum during the thawing process can denature immunoglobulins and affect the quality.

- b. Ingestion failure
  - (1) Poor udder or teat conformation or poor mothering ability make it difficult for the calf to ingest adequate amounts of colostrum in a timely fashion.
  - (2) Maternal periparturient disease (e.g., milk fever, calving injury) interferes with timely consumption of adequate amounts of colostrum, particularly in an unsupervised range environment.
  - (3) Poor neonatal vigor. The time for the calf to stand, find the teat, and suckle successfully varies between breeds. Holstein calves are well known for their poor neonatal vigor and FPT is almost certain if they are left on their own to suckle from the dam. Therefore, tube feeding of colostrum with an esophageal feeder within hours of life should be standard practice on most large dairy farms.
  - (4) Congenital musculoskeletal abnormalities (e.g., arthrogryposis, contracted tendons) prevent successful teat seeking and/or suckling and such calves should receive colostrum via a bottle or esophageal feeder.
- c. Absorption failure
  - (1) Neonatal asphyxia (dystocia). Severe or prolonged dystocia can produce neonatal asphyxia, which has adverse effects on multiple organs, including the gastrointestinal tract. Associations between postnatal acidosis and FPT have been reported in calves.
  - (2) Method of feeding affects passive transfer of immunoglobulin. Efficiency of absorption is higher with natural suckling than with bottle feeding or use of an esophageal feeder; however, in Holstein calves with poor neonatal vigor, the advantages of using an esophageal feeder far outweigh the disadvantage of less efficient immunoglobulin transfer.
  - (3) Extremes in environmental temperatures apparently affect the efficiency of immunoglobulin transfer across the intestinal epithelium because FPT is more prevalent during such environmental extremes.
  - (4) Absence of dam. There is evidence that calves will ingest more, and achieve higher serum immunoglobulin concentrations, if they are fed in the presence of their dams.
  - (5) Other factors that may affect efficiency of absorption include prematurity (immature gastrointestinal tract) and genetic variation in the efficiency of immunoglobulin transfer.

### C. Diagnostic plan and laboratory tests

1. Indications for testing
  - a. Individual testing is often part of routine screening of all newborn animals, and is a common practice on stud farms. It is also used for evaluation of a sick neonatal animal presented for treatment.
  - b. Herd testing. Tests for FPT can also be employed at the herd level to determine if FPT is contributing to unacceptably high morbidity and mortality in a herd. Immunoglobulin concentrations usually reflect passive transfer until the neonate is 8 days old; therefore, herd screening can be carried out on all animals younger than 8 days of age.
2. Timing
  - a. Traditional testing. Testing is most commonly conducted when the calf or foal is 18–24 hours of age. If FPT is detected at this stage, it can only be rectified by the intravenous administration of plasma or whole blood.
  - b. Early testing. If the foal suckled by 2 hours of age, passive transfer status can be assessed 8–12 hours after birth, prior to gut closure. If FPT is detected at this stage, an alternative source of colostrum can be administered in an attempt to achieve adequate passive transfer. Passive transfer status should be reassessed when the foal reaches 18–24 hours of age.

3. Laboratory tests used to screen for **FPT**

## a. Immunoglobulin concentration

## (1) Traditional testing

(a) Calves. The IgG concentration that is generally considered protective in calves raised under average management conditions is 1000 mg/dl; therefore, FPT is diagnosed if the IgG concentration of a calf is less than 1000 mg/dl.

(b) Foals. There are two cutoff points for FPT: one for foals that are sick at the time of testing and are being admitted to a referral center (less than 800 mg/dl), and one for foals that are healthy at the time of testing and are being screened on the farm (less than 400 mg/dl).

(2) Early testing. In foals, an IgG concentration of less than 200 mg/dl at 8–12 hours of age is considered presumptive evidence of FPT.

b. Single radial immunodiffusion (SRID) test. SRID represents the "gold standard" for assessing passive transfer in both horses and cattle and is the yardstick to which all other tests are compared. It is technically difficult to perform and results are not available for 24 hours; therefore, it is generally not used in the field.

c. Total serum protein (TSP) or Total solids (TS) test. This test is a useful and inexpensive way of assessing passive transfer status in calves, but its utility has been questioned in foals. A TS concentration of less than 5.0 g/dl generally indicates FPT in the calf. TS concentration should be interpreted with caution in the dehydrated calf; a TS greater than 5.0 g/dl in a dehydrated animal may in fact indicate FPT.

d. Globulin concentration from a biochemistry profile can serve as an indicator of immunoglobulin concentration. Approximately 1.5 g/dl of the globulin measurement represents the nonimmunoglobulin component and the remainder represents the immunoglobulin fraction. Therefore, in a calf with a globulin concentration of 1.8 g/dl, the immunoglobulin fraction is approximately 0.3 g/dl (1.8–1.5), or 300 mg/dl, and likely indicates FPT.

e. Zinc sulfate turbidity (ZST) test. The ZST test is used in both cattle and horses. A commercial test kit is available for horses or the reagent can be prepared. Zinc ions in the zinc sulfate solution combine with immunoglobulins to form a precipitate in serum; the more the precipitate at a given concentration of zinc sulfate, the higher the immunoglobulin concentration.

f. Sodium sulfite turbidity (SST) test. This test operates on the same principle as the ZST test, but is used primarily in calves.

g. Glutaraldehyde coagulation (GCT) test. This test is used in both calves and foals and is based on the ability of glutaraldehyde to react with gamma globulin, forming a solid clot. Serum or whole blood may be used, depending on the test kit. Unfortunately, test sensitivity and specificity are low when this test is performed on whole blood in the bovine species, probably because fibrinogen and other clotting factors interfere with test accuracy. Therefore, the GCT cannot be endorsed as a screening test.

h. Enzyme-linked immunosorbent assay (ELISA) is designed for the semiquantitative measurement of IgG in foal serum or plasma. The test uses a color spot with calibration standards corresponding to 200, 400, and 800 mg/dl of IgG. The assay takes 15 minutes to perform and results correspond well to those obtained with SRID.

i. Latex agglutination test. A commercial latex agglutination test is available for horses. The degree of agglutination between IgG in serum or blood and latex beads coated with antibody to equine IgG is used to estimate the IgG concentration.

j.  $\gamma$ -Glutamyl transferase (GGT) activity is used as an indicator of passive transfer status in the calf. Colostral GGT concentration in the bovine is about 300 times the serum GGT concentration. CCT from colostrum is absorbed along with other macromolecules during the period when the gut is open. CCT activity is at its peak when the calf is 24–48 hours of age; a GGT value of greater than 300 IU/L indicates that the calf has consumed colostrum.

4. Assessing colostral quality. **Colostrometers** (modified hydrometers) are available to assess colostral quality in both horses and cattle. There is an excellent correlation be-

tween colostral specific gravity and colostral immunoglobulin concentration in horses, but the strength of this association in cattle is weak.

a. Bovine colostrum. The literature and companies that manufacture colostrometers for commercial purposes state that bovine colostrum with a specific gravity greater than 1.050 is of satisfactory quality (i.e., the IgG concentration should be greater than 50 mg/ml). Recently this criteria has been shown to be inaccurate; the colostrometer will classify nearly 75% of low-quality colostrum as satisfactory using this standard.

b. Equine colostrum with a specific gravity of 1.060 (using the equine colostrometer) is usually classified as satisfactory, whereas samples with a specific gravity of greater than 1.090 are ideal. It is important to recognize that milk has a specific gravity of 1.040.

**D. Therapeutic plan**

1. Diagnosis within 12 hours of birth. If FPT is diagnosed or suspected less than 12 hours after birth, oral supplementation of IgG is indicated.

a. Foals. All foals receiving oral supplementation should be retested at 24 hours of age.

(1) Equine colostrum from a colostrum bank should be used. Banked colostrum should have a minimum specific gravity of 1.060 (and ideally, a specific gravity greater than 1.090) and the foal should receive 1–2 L in 500-ml increments administered 1 hour apart via nurse bottle or nasogastric feeding tube. Administering colostrum in this way should provide at least 1 g/kg of immunoglobulin to the foal.

(2) Alternative sources of immunoglobulin include bovine colostrum, equine plasma or serum, and commercially available lyophilized or concentrated IgG products.

(a) Bovine colostrum can be safely administered to foals; usually 4 L is administered in the first 24 hours of life. Bovine immunoglobulins have a very short half-life in the foal and may not protect the foal against pathogens unique to the equine environment (e.g., *Actinobacillus equuli*). However, most colostrum-deprived foals that receive bovine colostrum do not succumb to sepsis.

(b) Equine plasma and serum have very low immunoglobulin concentrations, so extremely large volumes are required to achieve adequate passive transfer.

(c) Commercial products. If the foal is treated with a concentrated commercial product, it should receive at least 1 g/kg of IgG (i.e., approximately 40 g for the average 40-kg foal).

b. Calves should be fed fresh or frozen first-milking colostrum from a third or greater lactation cow.

(1) Holstein calves. At least 28 L of colostrum should be administered via esophageal feeder in the first feeding.

(2) Other breeds. Calves should receive colostrum in amounts equal to 10% of their body weight in the first 24 hours, with at least 2 L being fed in the first 6 hours of life.

2. Diagnosis 18 or more hours after birth. If FPT is diagnosed 18 or more hours after birth, intravenous supplementation of IgG is indicated.

a. Foals

(1) Sources of immunoglobulin

(a) Commercial products. Advantages of commercial products are that they are free of alloantibodies and infectious agents and generally provide a known quantity of IgG. Some products originate from horses immunized with endotoxin or with specific pathogens (e.g., *Rhodococcus equi*). The major disadvantage of commercial products is that they may lack antibodies specific to pathogens in the foal's environment.

(b) Plasma harvested from a local donor. Harvested plasma provides specific protection to local pathogens, but harvesting is time consuming. Donors

should test negative for equine infectious anemia and should be screened by a blood-typing laboratory to ensure that they are negative for Qa/Aa alloantibodies and alloantigens.

(2) Administration

(a) The volume of plasma required depends on the magnitude of the immunoglobulin deficiency, the weight of the foal, and the immunoglobulin concentration in the donor plasma. Preexisting sepsis dramatically alters the distribution and catabolism of antibody in plasma and generally increases the amount required to achieve adequate passive transfer.

(i) A general guideline is to administer 200–400 mg IgG/kg; for plasma of average quality, this translates to 20–40 ml/kg. In a healthy foal of average weight, administration of 20 ml/kg of plasma (1 L) will raise the IgG concentration by approximately 200 mg/dl.

(ii) The highest concentrations of IgG are attained 1–3 hours posttransfusion, but it is best to assess the effects of plasma administration 24 hours posttransfusion, after redistribution has occurred to extravascular sites.

(b) Plasma should be administered through an in-line filter. The first 50 ml is administered slowly and the foal is closely monitored for tachypnea, tachycardia, or altered behavior. If no adverse reactions are observed, plasma is administered at a rate of 20 ml/kg/hour (1 L/hour for a 50 kg foal).

b. Calves

(1) Sources of immunoglobulin include plasma and whole blood. Whole blood transfusions are frequently used in calves because whole blood is easier and less expensive to harvest than plasma.

(2) Administration. The principles of administration are the same as for foals.

The recommended volume of blood to administer is 25 L for the average calf with FPT.

c. Lambs, piglets, and goat kids. Bovine colostrum is frequently used to supplement immunoglobulin in lambs, piglets, or goat kids if dam colostrum is not available. Anemia is occasionally reported in lambs fed bovine colostrum; the anemia has been attributed to immune complex attachment to the lamb's erythrocytes, resulting in the removal of the erythrocytes from the circulation.

## E. Prevention

1. Foals

a. **Prophylactic treatment.** Colostral IgG content should be evaluated using a colostrummeter to predict the risk of FPT in the foal. If the colostral specific gravity is less than 1.060, some degree of FPT can be anticipated and should be corrected prophylactically by either providing additional high-quality colostrum or by transfusing the foal with plasma.

b. Good management practices. Some of the factors predisposing to FPT can be circumvented by early intervention and careful management. Measures include identifying mares that dripped colostrum prior to parturition, attending foaling to ensure colostral ingestion by 2–3 hours of age, and screening of high-risk foals with doubtful nursing histories.

c. Establishment of a **colostrum bank**. A colostrum bank should be established by collecting 200–250 ml of colostrum from the mare within the first 3 hours of foaling, after the foal has suckled several times. Colostrum for the colostrum bank should be collected from the teat opposite to the one first nursed by the foal.

(1) Ideally, banked colostrum should have a high IgG concentration (i.e., a specific gravity greater than 1.090) and be free of anti-red cell antibodies to avoid neonatal isoerythrolysis.

(2) Colostrum can be stored frozen for 18 months without losing significant amounts of antibody.

2. Calves

a. Force-feeding of **colostrum**. Producers should be encouraged to observe early nat-

ural suckling or to force-feed colostrum in the first 6 hours of life. The calf should receive at least 10% of its body weight in colostrum in the first 24 hours of life and ideally, 2 liters should be consumed in the first feeding.

(1) Holstein calves. It is common practice to feed Holstein calves 2.8–3 liters of colostrum via esophageal feeder in the first 2 hours of life.

(2) Calves on farms with unacceptably high infectious disease prevalence should be force fed colostrum and screened to quantify passive transfer status.

b. Although the colostrumeter has been used in the past to select colostrum with a specific gravity of 1.050, the accuracy of this method has recently been questioned. Current recommendation is to discard colostrum from cows producing more than 8.5 kg in their first milking.

c. Because pooled colostrum is notoriously low in immunoglobulin concentration, the practice of feeding pooled colostrum to calves should be discouraged.



## SEPTICEMIA AND FOCAL INFECTION

### A.

Introduction. Septicemia and focal infection are major causes of morbidity and mortality in neonatal foals and calves. FPT and unsanitary management practices are important factors predisposing the neonatal foal or calf to septicemia. The early signs of neonatal septicemia are subtle and nonspecific and are often missed by the owner of the foal or calf. Consequently, many septicemic neonates are presented with well-established infections involving multiple organ systems; these animals have a poor prognosis.

### B.

Etiology, pathogenesis, and predisposing factors

1. Etiology. Gram-negative aerobic bacteria are the predominant cause of septicemia in neonatal foals and calves; however, aerobic gram-positive infections and **anaerobic** infections have been documented.

a. *Escherichia coli* is the bacterial agent isolated most frequently from septicemic foals and calves.

b. Other commonly isolated bacterial agents include *Actinobacillus* species (foals), *Pasteurella* species (calves and foals), *Klebsiella* species (calves and foals), and *Salmonella* species (calves and foals).

c. In addition, there are sporadic reports of the following agents being recovered: *Pseudomonas* species, *Listeria monocytogenes*, *Clostridium perfringens*, *Clostridium septicum*, *Streptococcus* species, and *Staphylococcus aureus*. In foals, streptococci are usually recovered in conjunction with gram-negative bacteria, but have been isolated in pure culture from foals with septic pharyngitis, osteomyelitis, and large subcutaneous abscesses. Polymicrobial infections are documented with some frequency in calves.

2. Pathogenesis. Most neonatal infections are caused by opportunistic bacteria residing in the genital tract, on the skin, or in the environment of cattle and horses.

a. In **utero-acquired** infections may ascend from the vagina, occur via hematogenous spread, or spread directly from the uterine wall. Clinical signs are evident during the first 24 hours of life.

b. **Infections** acquired during delivery usually occur in stressed foals and should be suspected when **meconium-contaminated** amniotic fluid or a meconium-stained foal is observed. Portals of entry include the respiratory and digestive tract or the umbilicus.

c. **Infections** acquired after **birth** usually manifest themselves when the neonate is 48–96 hours old and are the result of inadequate passive transfer of colostral immunoglobulin, poor husbandry practices, endemic infectious disease on the farm, or predisposing disease conditions.

3. Predisposing factors. There are a number of periparturient factors that increase the risk of septicemia in the neonate.

- a. Bacterial placentitis is an important risk factor in horses. Premature lactation, purulent vaginal discharge, premature delivery, and an abnormal placenta should alert the clinician that bacterial placentitis may be present. The foal may acquire infection from the mare with bacterial placentitis transplacentally, or from contaminated discharge present in the birth canal. In addition, premature lactation associated with bacterial placentitis results in poor colostrum quality and low serum immunoglobulin concentrations in the foal.
- b. **Perinatal** stresses (e.g., chronic in utero hypoxia, acute birth asphyxia, prematurity, dystocia) also increase the susceptibility of the neonate to infection. Compromised foals may be unable to stand and nurse causing a delay in colostrum ingestion, low serum immunoglobulin concentrations, and an increased susceptibility to infection.
- c. Overcrowding, poor ventilation, and contamination of the environment with pathogenic bacteria (e.g., *Salmonella* species) also predispose the neonate to infection.

### C. Clinical findings

1. **Septicemia.** Clinical signs of septicemia in the neonate vary according to the stage of disease and the site of localized infection.
  - a. The early signs of septicemia in neonatal calves and foals are vague and nonspecific and are often indistinguishable from noninfectious diseases or focal infections (e.g., diarrhea). Early clinical signs may include depressed mentation (lethargy, poor suckle reflex, weakness, recumbency), diarrhea, and dehydration.
  - b. Body temperature abnormalities may include fever or hypothermia; however, a normal rectal temperature should not be used to exclude a diagnosis of septicemia.
  - c. **Abnormal** mucous membranes are usually present in septicemic neonates. Coloration may range from a muddy red-gray, to mottled, pale, or cyanotic. A toxic line rimming the incisors is occasionally observed in foals. The capillary refill time is usually delayed (>2 seconds) and **scleral** injection is common. Careful inspection may reveal petechiation of the ears, sclera, vulvar, or buccal membranes and suggests presence of disseminated intravascular coagulation (DIC).
2. **Localized** infection. Localization of infection in various organs of septicemic neonates can cause a variety of clinical signs.
  - a. Pneumonia may occur as a complication of septicemia. Cough, nasal discharge, tachypnea, dyspnea, and fever support the diagnosis, but in many septicemic neonates, respiratory rates and lung sounds are normal despite extensive lung pathology. Therefore, chest radiographs are indicated in all septicemic neonates.
  - b. Diarrhea may occur secondary to septicemia or enteritis caused by enteropathogens. Enteritis may provide a portal of entry for opportunistic bacteria.
  - c. Septic meningitis is a common complication of septicemia in the neonatal animal. Early signs include lethargy, depression, aimless wandering, and abnormal vocalization. Signs usually progress to diffuse cranial nerve deficits; apparent blindness; **truncal** and **limb** ataxia; weakness; recumbency; and coma, seizures, or **both**.
  - d. Septic arthritis and **osteomyelitis** are common, debilitating **sequelae** of neonatal septicemia. Acute lameness, periarticular edema, joint capsule distention, or **physical** pain in a farm animal neonate should alert the clinician to the possibility of bone or joint infection.
  - e. **Uveitis** is diagnosed based on the presence of hyphema, hypopyon, or the accumulation of fibrin in the anterior chamber of the eye. Additional clinical manifestations include blepharospasm, photophobia, excessive tearing, miosis, and ciliary and **episcleral** injection.
  - f. Omphalitis is characterized by heat, pain, swelling, and purulent discharge from the umbilicus (see also VI A). However, the absence of **external** signs of umbilical involvement should not preclude a diagnosis of omphalitis (ultrasonographic evaluation of the umbilical structures and deep abdominal palpation will confirm involvement of **internal** structures).

3. **Septic shock.** Neonatal animals frequently present in septic shock.
  - a. The early stage of septic shock (hyperdynamic septic shock, septicemia without circulatory collapse) is characterized by injected mucous membranes, a normal capillary refill time and blood pressure, and warm extremities. Localizing signs of infection may or may not be present. Prompt and aggressive intervention at this time can result in a favorable outcome.
  - b. The late stage of septic shock (hypodynamic septic shock) is characterized by tissue hypoperfusion. Clinical signs include cold extremities, sluggish capillary refill, hypotension, pale gray mucous membranes, and markedly altered mentation. At this stage, multiorgan failure is present and therapeutic intervention is often futile.

### D. Diagnostic plan

1. **Routine laboratory testing**
  - a. Leukogram abnormalities are commonly encountered in septicemic neonates. The white blood cell (WBC) count may be normal early in the course of sepsis, but an increase in the number of band neutrophils or toxic changes in neutrophils (e.g., Dohle's bodies, toxic granulation, vacuolization) are usually present. Neonatal farm animals with well-established septicemia generally have a profound **leukopenia** and neutropenia accompanied by toxic changes in their neutrophils.
  - b. Fibrinogen concentration can be used to determine whether infection was acquired pre- or postnatally. A foal infected *in utero* may have a fibrinogen concentration as high as 1000 mg/dl at birth. Moderate increases in fibrinogen concentration (to approximately 400–500 mg/dl) are expected in neonates with early postnatal infections, but with chronicity, or well-established focal infection, the concentration increases dramatically.
  - c. **Blood glucose.** Hypoglycemia is a common finding in the neonate with septicemia and has been attributed to decreased feed intake, low hepatic glycogen stores, and abnormal glucose metabolism caused by endotoxemia (depressed hepatic gluconeogenesis and increased peripheral uptake of glucose).
  - d. **IgG** determination should be carried out in all neonatal farm animals suspected of being septicemic because there is a strong association between poor passive transfer of colostral immunoglobulin and septicemia.
  - e. Arterial blood gas analysis is an important component in the evaluation of a septicemic foal or calf. Hypoxemia and a metabolic acidosis are frequently present.
  - f. Serum biochemistry profile. Biochemical abnormalities that are detected with some frequency in the septicemic neonate are **azotemia**, which is attributed to poor renal perfusion, and hyperbilirubinemia, which is usually ascribed to **endotoxin-induced cholestasis**. In addition, foals or calves with severe diarrhea may exhibit electrolyte abnormalities (e.g., hyponatremia, hypochloremia, **hypokalemia**).
2. **Cultures**
  - a. **Blood cultures.** A positive blood culture is required for a definitive **antemortem** diagnosis of septicemia, but it may take as long as 48–72 hours before a culture can be determined to be positive. Blood cultures should be repeated in any hospitalized foal that deteriorates clinically, has a fever spike, or exhibits a dramatic change in its WBC picture.
    - (1) **Technique.** Blood cultures are easy to perform, but attention should be paid to sterile technique. The hair should be clipped and the venipuncture site surgically prepared. Depending on the culture type, a set amount of blood is withdrawn and transferred in an aseptic manner to the culture bottle or vial. A clean needle should be used to transfer the blood into the bottle.
      - (a) Aerobic and anaerobic cultures are often performed.
      - (b) Some authors recommend that at least two cultures spaced 1 hour apart be performed to maximize the chances of obtaining a positive result. However, in human neonates, a single culture has been shown to detect the presence of bacteria in the blood 91.5% of the time.
    - (2) **Sensitivity.** Although previous antimicrobial use may cause false-negative blood culture results, the sensitivity of blood cultures in foals has been remarkably good, ranging from 61%–80%.

- b. Culture from sites of focal infection. Bacterial cultures can also be performed on fluid obtained from sites of focal infection (e.g., cerebrospinal fluid, joint fluid, peritoneal fluid, tracheal fluid). In foals with in *utero*-acquired infections, blood cultures are frequently negative because infection occurs via inhalation or ingestion. In such cases, it may be useful to culture the pharynx, trachea, external ear canal, and stomach contents.
  - (1) Culture of the same pathogen from more than two sites of focal infection supports a diagnosis of bacteremia.
  - (2) Recovery of the same pathogen from blood and a site of focal infection lends support to the contention that the pathogen recovered from blood is in fact significant.
3. Sepsis scoring systems. Because no single laboratory test has emerged as being completely reliable for the early diagnosis of septicemia in farm animal neonates, various scoring systems and predictive models using easily obtainable historic, clinical, and clinicopathologic data have been developed for this purpose. In general, the goal of these mathematical models is to identify septicemic neonates early in the course of disease when appropriate therapeutic intervention would most likely result in a favorable outcome.
  - a. **Laboratory** parameters incorporated in these models include neutrophil count, band neutrophil count, toxic changes in neutrophils, fibrinogen concentration, blood glucose, and IgG determination.
  - b. Clinical parameters that appear in most of these models are scleral injection, fever or hypothermia, and evidence of focal infection (e.g., uveitis, diarrhea, respiratory distress, joint effusion).
  - c. Historic data incorporated in some of the models include history of vaginal discharge, systemically ill mare, general anesthesia in the mare, induction of parturition, and premature birth (i.e., less than 320 days' gestation).

#### E. Therapeutic plan

1. General supportive care
  - a. Respiratory support. Hypoxemia must be corrected and respiratory failure treated, if present (see II D 8).
  - b. Fluid resuscitation. Hypovolemic shock and hypoglycemia should be treated with appropriate warmed intravenous fluids.
    - (1) Alternating lactated Ringer's solution with 5% dextrose, or administering 2.5% dextrose and 0.45% saline, is often sufficient.
    - (2) If metabolic acidosis is severe, or **uncorrectable** by volume expansion with balanced polyionic solutions, intravenous infusion of isotonic (1.3%) sodium bicarbonate solution may be required.
  - c. Intravenous plasma should be administered to restore circulating blood volume, osmotic pressure, and immunoglobulin concentrations.
  - d. Positive inotropic agents. For circulatory embarrassment that persists after rehydration, positive inotropes should be administered. **Dopamine** (2–5  $\mu\text{g/kg/min}$  by infusion) is the drug of choice because it increases cardiac output and causes splanchnic and renal vasodilation.
  - e. **Nonsteroidal anti-inflammatory drugs (NSAIDs)** have been shown to counteract a number of the clinical and laboratory changes associated with endotoxemia, including decreased cardiac output and hypotension. **Flunixin meglumine** (0.25–1.1  $\text{mg/kg}$ , intravenously or intramuscularly every 8 hours) has been recommended.
  - f. Nutritional support. Foals that are unable to nurse should be fed via a nasogastric tube using the recommendations given in II D 4. Total or partial parenteral nutrition is indicated in foals that cannot be fed orally.
2. Control of generalized infection
  - a. General principles
    - (1) Antibiotic selection. When possible, antibiotic selection is made based on the results of blood culture and sensitivity testing. However, because blood culture results are not returned for several days, and the offending agent may

not be recovered, empiric therapy is usually initiated and modified later if needed. Broad-spectrum bactericidal drugs are indicated in the treatment of septicemic neonates for the following reasons:

- (a) Gram-negative and polymicrobial infections should be anticipated
- (b) Septicemia in neonates is rapidly progressive
- (c) Many septicemic neonates are neutropenic
- (d) Immune function in neonates is usually compromised by stress and FPT
- (2) Antibiotic administration. Initially, the intravenous route is preferred for antibiotic administration because peripheral circulation may be compromised, making absorption from other routes inconsistent.
- (3) Duration of therapy. The recommended duration of therapy for suspected but undocumented sepsis is 7–10 days. Neonates with positive blood cultures and no evidence of focal infection should be treated for at least 2 weeks, and those with localized infections should be treated for 3–4 weeks.
- b. Antibiotic therapy in foals. Selection of antimicrobials should be based on the results of an antimicrobial susceptibility pattern; however, until culture results are returned selection of drugs will be somewhat empirical.
  - (1) A combination of a  $\beta$ -lactam antibiotic (e.g., penicillin, ampicillin) and an aminoglycoside (e.g., gentamicin, amikacin) usually provides good broad-spectrum coverage. Many clinicians prefer amikacin because it is less nephrotoxic and is less likely to be associated with development of resistant bacterial infections. If possible, peak and trough serum concentrations of aminoglycosides should be monitored to ensure that the drug dose and dosing interval are appropriate. General doses are as follows:
    - (a) **Gentamicin:** 22  $\text{mg/kg}$ , intramuscularly or intravenously, every 8–12 hours or 3.3  $\text{mg/kg}$ , intramuscularly or intravenously, every 12 hours
    - (b) **Amikacin:** 7  $\text{mg/kg}$ , intramuscularly or intravenously, every 8–12 hours or 10  $\text{mg/kg}$ , intramuscularly or intravenously, every 12 hours
  - (2) Cephalosporins. Cefotaxime or ceftiofur can be used in the empiric treatment of septic neonates. General doses are as follows:
    - (a) Cefotaxime: 20–30  $\text{mg/kg}$ , intravenously or intramuscularly, every 8 hours
    - (b) Ceftiofur: 2.2–6.6  $\text{mg/kg}$ , intramuscularly or intravenously, every 8–12 hours
  - (3) Other drugs. The following drugs are also listed for the treatment of septicemic foals.
    - (a) **Trimethoprim-sulfonamide** combinations: 15  $\text{mg/kg}$ , intravenously or orally every 12 hours (resistance to this drug is wide spread)
    - (b) **Chloramphenicol:** 25–50  $\text{mg/kg}$ , intravenously or orally, every 6 hours
    - (c) **Ticarcillin-clavulanate:** 50  $\text{mg/kg}$ , intravenously, every 6–8 hours
- c. Antibiotic therapy in calves is simplified by the limited number of choices available.
  - (1) **Ceftiofur** (5  $\text{mg/kg}$ , administered intravenously or intramuscularly every 8–12 hours) is widely used to treat calf septicemia, as are the potentiated **sulfonamides** (15  $\text{mg/kg}$  administered orally, intramuscularly, or intravenously every 12 hours).
  - (2) In Canada, **ampicillin sulbactam** (6.6  $\text{mg/kg}$  administered intramuscularly every 12–24 hours) has been used successfully to treat neonatal calf septicemia.
  - (3) Aminoglycosides are generally avoided because of prolonged tissue residues (18 months in the kidney) and because their use is not endorsed by the National Cattlemen's Association. However, some clinicians still use gentamicin (3–5  $\text{mg/kg}$ , administered intravenously or intramuscularly every 12 hours) if they can obtain assurance from the client that the animal in question will not enter the food chain for at least 18 months.
  - (4) **Fluoroquinolones** are banned for use in cattle in the United States, but **enrofloxacin** (2.5–5  $\text{mg/kg}$  orally every 24 hours) is used widely in other countries to treat septicemia in neonatal calves.

- (5) Tetracyclines and **sulfonamides** are used by producers, but resistance to these drugs is widespread.
3. Treatment of focal infections
- Septic meningitis (see also Chapter 11 I E)
    - Antibiotic therapy
      - Septic meningitis is treated with bactericidal antimicrobials that penetrate the blood–brain barrier (**e.g.**, trimethoprim–sulfonamide combinations or third-generation **cephalosporins**).
      - Combination therapy using a  **$\beta$ -lactam** antibiotic or **trimethoprim–sulfonamide** with an aminoglycoside is also beneficial as a result of synergistic interactions, despite poor penetration of aminoglycosides into the **CSF**.
      - Although chloramphenicol readily crosses the blood–brain barrier, it is bacteriostatic against gram-negative enteric bacteria and is not recommended for the treatment of bacterial meningitis.
    - Anticonvulsants** (**e.g.**, diazepam, phenobarbital) and **NSAIDs** (**e.g.**, flunixin meglumine) may also be indicated.
  - Septic arthritis or **osteomyelitis**. Therapeutic measures include:
    - Systemic antibiotic therapy
    - Assurance of adequate serum immunoglobulin concentrations
    - Analgesic therapy
    - Drainage and removal of debris from the joint and adjacent tissues (lavage with sterile polyionic fluids)
    - Articular rest
    - Exogenous sodium **hyaluronate** or **polysulfated glycosaminoglycan** therapy
    - Surgical debridement, installation of a sterile drain, and immobilization of the limb with a Robert-Jones splint bandage (in cases of osteomyelitis with evidence of bone sequestration or **osteolysis**)
  - Uveitis. Treatment should include systemic antimicrobial therapy and local therapy to prevent permanent ocular damage: A mydriatic (**e.g.**, atropine), topical ophthalmic corticosteroid, systemic NSAID, and broad-spectrum ophthalmic preparation are indicated.
  - Omphalitis. Treatment is discussed in VI A.

## F. Prognosis

- The overall **survival** rate for septicemic neonates is less than **60%**, but early recognition of sepsis and appropriate and aggressive intervention improve the outcome.
  - A septicemic large animal neonate with FPT and **evidence** of multiple organ involvement should always be given a guarded prognosis.
  - A neonate with a negative blood culture but evidence of focal infection (**e.g.**, pneumonia, diarrhea) has a more favorable prognosis.
  - Appropriate and early therapeutic intervention in foals with **in utero-acquired** infections often results in a favorable outcome: survival rates greater than 75% have been quoted for this group.
- The **long-term prognosis** for **future** athletic performance is guarded if **multifocal** bone or joint disease is diagnosed.

**G.** Prevention. Management of the mare with placentitis can decrease the risk of premature delivery and postnatal infection. **Aspergillus** species,  **$\beta$ -hemolytic streptococci**, and **E. coli** are the organisms isolated most frequently from mares with placentitis. Treatment of placentitis includes the use of antimicrobial **agents**, anti-inflammatory drugs, **progestins**, and stall rest

- Antimicrobial agents are usually selected based on results of culture and sensitivity. Trimethoprim–sulfonamide (25–35 **mg/kg** every 12 hours) is a good antimicrobial to start with because high concentrations are achieved in the placenta, **allantoic** fluid, amniotic fluid, and fetal serum.
- NSAIDs**, such as **phenylbutazone** (4 **mg/kg** orally every 24 hours) or **flunixin meglumine** (1 **mg/kg** orally, intravenously, or intramuscularly every 12 hours) may reduce

uterine inflammation and uterine production of prostaglandin **F2 $\alpha$** , thereby decreasing the risk of premature delivery.

- Supplemental progestin therapy with altrenogest (0.044 **mg/kg** every 24 hours) has been employed to maintain pregnancy in mares with placentitis. Although this **progestin** will maintain pregnancy in ovariectomized mares, the efficacy of this regimen in late-term mares with high-risk pregnancy is unknown.

## VI. UMBILICAL ABNORMALITIES

- A.** Umbilical remnant infections. Infection may involve the urachus, umbilical veins (**omphalophlebitis**), one or both umbilical arteries (omphaloarteritis), or many structures (omphalitis, umbilical abscess).
- Clinical findings may include umbilical enlargement, pain on palpation, patent **urachus** (common in foals, rare in calves), or purulent discharge. The internal or **intra-abdominal** umbilical structures may be the only structures affected in foals, making infection difficult to detect on physical examination.
    - As with most neonatal infections, the first signs noted are decreased suckling and depression. Other abnormalities may include fever, dysuria, **pollakiuria**, and **tenesmus**.
    - Deep abdominal palpation can be used to evaluate the internal umbilical structures, particularly in calves. Enlargement of the umbilical vein may be palpable coursing cranially toward the liver; enlarged umbilical arteries may be palpable coursing caudally toward the bladder. Palpation may elicit a grunt and abdominal splinting may be noted in calves with a septic umbilicus and associated peritonitis.
  - Pathogenesis. Infection may originate following contamination of the external **umbilicus** after birth or result from seeding from other sites during periods of septicemia. Bacteria may localize in the umbilical vessels, urachus, bladder, or interstitial tissues and the infection may extend into the peritoneal cavity or progress to a generalized septicemia. Urachal abscessation can cause the previously closed urachus to become patent externally or allow urine to leak subcutaneously or into the peritoneal cavity.
  - Diagnostic plan and laboratory tests
    - Routine laboratory tests. Clinicopathological alterations usually include **neutrophilia** with toxic changes in neutrophils and **hyperfibrinogenemia**.
    - Blood culture. Because of the association of umbilical remnant infections with septicemia, blood cultures should always be performed.
    - Ultrasonography** should be used to evaluate the extent of involvement of internal umbilical structures. An increased diameter, thickened wall, or abscesses may be visible. The procedure is usually carried out with the foal in lateral recumbency and the calf standing.
      - In foals, the umbilical arteries and vein can be followed from the external **umbilical** stump to the cranial aspect of the bladder and liver, respectively. The urachus can usually be visualized along with the umbilical arteries just caudal to the umbilical stump.
      - In calves, the umbilical arteries retract into the abdominal cavity and thus should not be identifiable in the umbilical stalk; they are most easily located along the apex of the urinary bladder. The umbilical vein of calves is scanned from the umbilical stalk to the liver along the right ventral abdomen. Urachal remnants can usually not be identified in normal calves.
  - Therapeutic plan. The treatment options for umbilical remnant infections are medical management or surgical resection.
    - Medical therapy consists of prolonged antibiotic administration (see V E 2) and encouragement of drainage. In one study, 50% of foals responded to medical therapy alone.

- (1) Frequent ultrasound examinations should be carried out to evaluate progress in all neonates treated medically.
  - (2) Risks associated with not removing infected remnants are the development of septic arthritis, pneumonia, peritonitis, or uroperitoneum from urachal rupture.
  - b. Surgery. Evidence of multisystemic infection, umbilical vein involvement, uroperitoneum from urachal rupture, or failure to respond to medical therapy are all indications for surgery.
5. Prevention
- a. Adequate passive transfer and a clean environment should be ensured to minimize the chances of septicemia and seeding of the umbilicus.
  - b. Proper postpartum care of the umbilical remnant decreases the chance of bacterial colonization. The following solutions have been used for dipping the umbilicus: 2% iodine, 1% povidone-iodine, and 0.5% chlorhexidine.
    - (1) In one study, chlorhexidine therapy caused the lowest bacterial counts on the umbilicus immediately posttreatment. Chlorhexidine also binds to the stratum corneum and has a longer residual effect than other treatments.
    - (2) The use of 7% iodine should be discouraged. Local tissue necrosis associated with application of 7% iodine may actually increase the prevalence of infection.

#### **B.** Patent **urachus** (see also II B 5)

1. Etiology and pathogenesis
  - a. Congenital patent urachus. The exact pathophysiologic mechanisms leading to the development of a congenital patent urachus have not been established. One theory is that excessive torsion of the umbilical cord in *utero* causes urachal obstruction, urine retention in the bladder, distention of the proximal urachus, and interference with urachal involution.
  - b. Acquired patent urachus. Reestablishment of urine flow after a normal urachal closure at birth is termed acquired **patent** urachus. Any insult that causes tension on the abdominal wall (e.g., prolonged recumbency, **tenesmus**, abdominal distention) or umbilical inflammation (e.g., **omphalitis**) may lead to the development of an acquired patent urachus.
2. Clinical findings
  - a. A diagnosis is usually made when urine is **observed** dribbling or flowing from the umbilical stump. Dermatitis may develop on the hindlimbs and ventral abdomen from urine scalding.
  - b. Fever, purulent discharge, and pain on palpation of the umbilicus suggest that the patent urachus is a **sequela** of an umbilical remnant infection.
3. Diagnostic plan
  - a. Contrast **cystography** can be used to confirm the diagnosis in cases where a patent urachus is suspected, but where urine is not obviously dribbling from the umbilical stalk.
  - b. CBC. A CBC should be performed to determine if there is intercurrent infection (findings would include **leukocytosis** and **hyperfibrinogenemia**).
  - c. **Serum IgG** concentration should be measured to determine if FPT is present.
  - d. **Ultrasonography** can be used to determine if the urachal patency is associated with infection of the umbilical remnants.
4. Therapeutic plan
  - a. Conservative management is used in cases of uncomplicated patent urachus occurring in foals younger than 5 days.
    - (1) Local therapy and removal of predisposing conditions are necessary.
    - (2) Cauterization of the urachus with silver nitrate sticks, 2% iodine, or local **injection** of procaine penicillin has been advocated to speed healing. These treatments should not be applied beyond the abdominal wall because they may cause urachal abscessation or cystitis.
    - (3) Careful monitoring of patients is indicated to identify infection.

- b. Surgical management is indicated for the following patients:
  - (1) Patients with persistent urine dribbling in spite of cauterization and resolution of predisposing factors (e.g., recumbency)
  - (2) Patients with involvement of other umbilical structures (demonstrated by ultrasound)
  - (3) Patients with subcutaneous or intra-abdominal urine accumulation resulting from a rent in the urachus
5. Prevention
  - a. The umbilicus should be allowed to rupture spontaneously.
  - b. Critically ill neonates should be restrained to prevent excessive tension on the ventral abdomen.

**C** Excessive bleeding from the umbilicus. Bleeding from the umbilicus may occur, particularly if it was cut or ligated. Occasionally, hemorrhage is severe enough to necessitate a blood transfusion. Rarely, hernoperitoneum will result from hemorrhage from an intra-abdominal umbilical vessel.

## STUDY QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE numbered answer or completion that is BEST in each case.

1. Which of the following conditions affecting neonatal foals is usually associated with a favorable long term outcome (i.e., a satisfactory performance animal)?

- (1) Hypoxemic-ischemic encephalopathy (HIE)
- (2) Prematurity with tarsal bone collapse
- (3) Septic arthritis
- (4) Twinning
- (5) Septic phylitis

2. Which of the following historic or laboratory findings would indicate that a prematurely delivered foal is endocrinologically mature ("ready for birth")?

- (1) Cesarean section at 322 days' of gestation
- (2) Total white blood cell (WBC) count less than 5000 cells/ $\mu$ L on day 3
- (3) A neutrophil-lymphocyte ratio greater than 2 at birth
- (4) A plasma fibrinogen concentration of 200 mg/dl on day 1
- (5) No change in the neutrophil-lymphocyte ratio in response to adrenocorticotrophic hormone (ACTH) administration

3. The bacterial agent that is cultured most frequently from neonatal calves and foals with septicemia is:

- (1) *Actinobacillus equuli*.
- (2) *Staphylococcus aureus*.
- (3) *Klebsiella pneumoniae*.
- (4) *Listeria monocytogenes*.
- (5) *Escherichia coli*.

4. Which one of the following antibiotics, or combination of antibiotic drugs, would be a rational first choice for treatment of a foal with clinical and laboratory findings indicating a diagnosis of septicemia?

- (1) Chloramphenicol
- (2) Oxytetracycline
- (3) Penicillin and amikacin
- (4) Lincomycin and spectinomycin
- (5) Ampicillin

5. Which one of the following antibiotics would be a rational first choice for treatment of a calf with clinical and laboratory findings indicating a diagnosis of septicemia?

- (1) Chloramphenicol
- (2) Oxytetracycline
- (3) Enrofloxacin
- (4) Ceftiofur
- (5) Erythromycin

6. In a study conducted in foals, which one of the following disinfectants was shown to cause the greatest decrease in bacterial count at the end of the umbilicus immediately post-dipping?

- (1) Dilute sodium hypochlorite
- (2) 0.5% Chlorhexidine
- (3) 7% Tincture of iodine
- (4) 2% Iodine
- (5) 1% Povidone-iodine

7. How much milk should a healthy 1-week-old foal weighing 60 kg consume in a 24-hour period?

- (1) 12 liters
- (2) 6 liters
- (3) 4 liters
- (4) 2 liters
- (5) 24 liters

8. Which one of the following statements pertaining to the feeding of bovine colostrum to neonatal foals is true?

- (1) Bovine colostrum should never be fed to foals because it causes severe bloating and diarrhea.
- (2) Bovine colostrum should never be used in foals because it often causes an immune-mediated hemolytic anemia.
- (3) Bovine colostrum prevents septicemia caused by *Actinobacillus equuli*, but not septicemia caused by *Escherichia coli*.
- (4) Bovine antibodies have a short half-life, but will protect the foal against septicemia most of the time.
- (5) Bovine colostrum cannot be used in foals because unrealistically large volumes are required to provide adequate protection.

9. Which one of the following laboratory findings likely indicates adequate passive transfer on routine screening of a healthy 2-day-old calf?

- (1) Total serum protein (TSP) concentration of 6.2 g/dl
- (2) Immunoglobulin C (IgG) concentration of 400 mg/dl
- (3)  $\gamma$ -Glutamyl transferase (GGT) activity of 23 IU/L
- (4) IgG concentration of 800 mg/dl
- (5) TSP concentration of 4.9 g/dl

10. Which one of the following drugs is contraindicated in treating a neonatal foal with coma, intermittent seizures, and oliguria following an acute asphyxial episode at birth (premature placental separation)?

- (1) Diazepam
- (2) Dimethylsulfoxide (DMSO)
- (3) Acepromazine
- (4) Furosemide
- (5) Dopamine

## ANSWERS AND EXPLANATIONS

1. The answer is 1 [I C 2 a]. With appropriate care foals with hypoxic-ischemic encephalopathy survive, and in the long term, this condition has little impact on performance. In contrast, foals with infectious or noninfectious orthopedic diseases have poor long term prognoses. Products of a twin pregnancy also have a grim prognosis as performance animals because they are small in stature and often suffer from noninfectious orthopedic conditions (e.g., tarsal collapse).

2. The answer is 3 [II A 2, E 2 b–c]. A neutrophil–lymphocyte ratio that is greater than 2 by 3 days of age indicates maturity of the adrenal–pituitary–hypothalamic axis and readiness for birth. In contrast, a white blood cell (WBC) count less than 5000 cells/ $\mu$ L in the first 3 days of life and no widening of the neutrophil–lymphocyte ratio in response to adrenocorticotrophic hormone (ACTH) administration indicates immaturity of the endocrine system and unreadiness for birth, as does a cesarean section performed at 322 days' of gestation. A fibrinogen concentration of less than 400 mg/dl at birth suggests that chronic in utero stress due to placentitis was probably not the cause of the premature delivery and, therefore, the fetus was probably not ready for birth.

3. The answer is 5 [V B 1 a]. *Escherichia coli* is the pathogen cultured most frequently (representing more than 50% of isolates) from septicemic farm animal neonates. *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Listeria monocytogenes* are isolated sporadically from septic calves and foals. *Actinobacillus equuli* is usually only found in foals.

4. The answer is 3 [V E 2 b (1)]. Both penicillin and amikacin are bactericidal drugs and the combination provides broad-spectrum coverage. Amikacin is preferred over gentamicin by many clinicians because it is less nephrotoxic and also because resistance is less likely. Chloramphenicol provides broad-spectrum coverage, but it is bacteriostatic and therefore not ideal for treating a rapidly progressing infection in a neonatal animal with an immature immune system. Resistance of septicemia pathogens to ampicillin and oxytetracycline is widespread.

5. The answer is 4 [V E 2 c]. Ceftiofur is a broad-spectrum bactericidal drug and many clinicians use it for the treatment of septicemia in neonatal calves. It is illegal to use chloramphenicol in cattle; therefore, this antibiotic would not be a good choice. Oxytetracycline is bactericidal but resistance is widespread. It is illegal to use enrofloxacin in cattle in the United States and there are some concerns that this antibiotic may cause joint cartilage abnormalities in rapidly growing young animals. Erythromycin is bacteriostatic and has a gram-positive spectrum of activity, so this drug would not be a good choice in a neonatal calf with a rapidly progressing gram-negative bacterial infection.

6. The answer is 2 [VI A 5 b]. In a study conducted in foals, application of 0.5% chlorhexidine to the umbilicus was shown to cause the lowest bacterial count on the umbilicus immediately post-treatment. The use of 7% tincture of iodine is discouraged; local tissue necrosis associated with the application of 7% iodine may actually increase the prevalence of infection.

7. The answer is 1 [II D 4 a]. A healthy newborn foal usually consumes approximately 20%–25% of its body weight in milk over a 24-hour period. Therefore, a healthy 1-week-old foal weighing 60 kg should consume 12 liters of milk over a 24-hour period ( $0.20 \times 60 = 12$ ).

8. The answer is 4 [IV D 1 a (2) (a)]. Although the immunoglobulins in bovine colostrum are rapidly catabolized in foals, bovine colostrum does provide protection against most pathogens capable of causing septicemia, with the exception of *Actinobacillus equuli*, a pathogen unique to the equine environment. Bovine colostrum is well-tolerated by foals and only occasionally causes diarrhea. There are no reports of hemolytic anemia in foals fed bovine colostrum, although anemia has been reported to occur in lambs. The volume of bovine colostrum required to confer protection in foals is approximately 4 liters, a volume that is easily achieved.

9. The answer is 1 [IV C 3]. A TSP concentration greater than 5.0 g/dl generally indicates ad-

equate passive transfer. A healthy 2-day-old calf with a total serum protein (TSP) concentration of 6.2 g/dl has adequate passive transfer. An immunoglobulin G (IgG) concentration of greater than 1000 mg/dl indicates adequate passive transfer, as does  $\gamma$ -glutamyl transferase (GGT) activity greater than 300 IU/L.

10. The answer is 3 [III F 1 a (3)]. Acepromazine, which may lower the seizure threshold and

cause systemic hypotension, further decreasing renal perfusion, is contraindicated in a neonatal foal with neurologic signs following an acute asphyxia episode at birth. Diazepam is frequently used for seizure control and dimethylsulfoxide (DMSO) is employed by many clinicians to treat cerebral edema. Furosemide is indicated as a diuretic in oliguric asphyxiated foals and dopamine infusion is advocated to increase renal blood flow.